Male Reproductive System

Physiological Anatomy of Male Sex Organs

As shown in ***Fig (1),*** the principal male organs in a human male reproductive system include:

1- Primary sex organ which is the male gonad or "Testis".

2- Secondary internal sex organs which include:

i- A system of ducts including the epididymis, and vas deferens.

ii- Accessory sex glands including seminal vesicles, prostate and the bulbouretheral (Cowper's) glands.

3- External copulatory organ the 'Penis'.

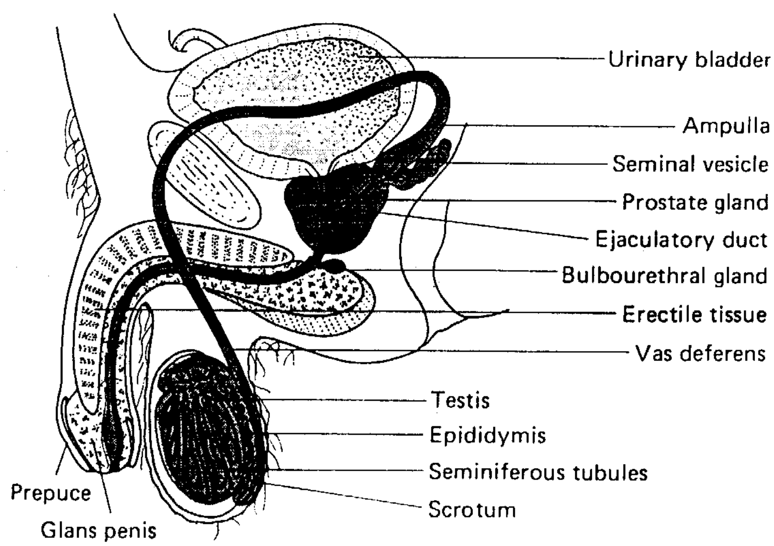


Fig. (1)

The Testis

functions:

1-Spermatogenesis : Formation of “spermatozoa”.

2-Endocrine function : Production of the male sex hormone "Testosterone", .

<u>Blood Supply of the testis:</u>

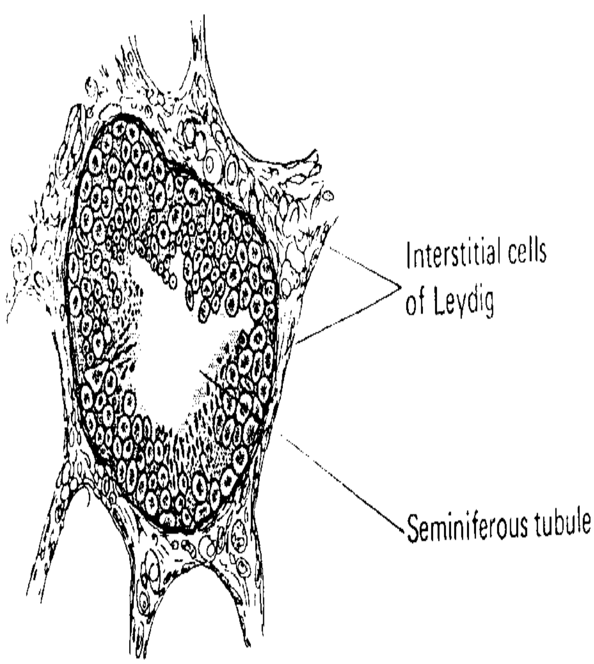
The testis is supplied by the spermatic arteries. These arteries are parallel but opposite in direction to the pampiniform plexus of the spermatic veins. This is a countercurrent system allowing exchange of heat and testosterone between the arteries and the venous plexus.

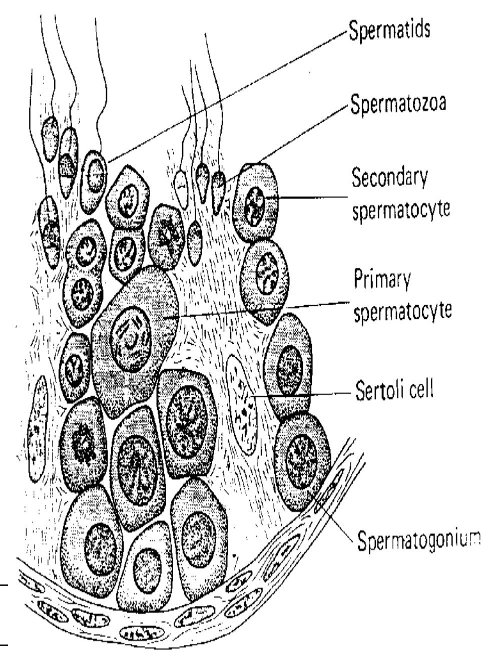
Stucture of the testis

A- Seminiferous tubules:

They are convoluted hollow tubules, lined with basement membrane. ***(Fig. 2).*** These tubules contain two types of cells:

1- Spermatogonia are primitive germ cells (sperm cell precursors) which lie close to the basement membrane. These cells divide to produce spermatozoa.





2- Sertoli cells which are large cells with a large amount of cytoplasm rich in glycogen. The Sertoli cells are closely related to the germ cells and extend

from the base of the seminiferous tubule to the lumen. . Tight-junctions exist between the neighboring Sertoli cells help to form the blood-testis barrier.

B- Interstitial cells of Leydig:

These are nests of cells between seminiferous tubules that secrete testosterone .

Spermatogenesis

It is the process of producing mature spermatozoa. From birth, the division of the germ cells is suppressed until puberty. At puberty , spermatogenesis begins and the original germ cells become known as Spermatogonia as shown in ***(Fig. 3).***

- The primary Spermatogonia start to proliferate by dividing mitotically to produce secondary Spermatogonia having the same diploid number of chromosomes (44 XY).
- The secondary Spermatogonia increase in size to form primary spermatocytes which divide meiotically to produce secondary spermatocytes, each carrying half the number of chromosomes (22 + X or 22 + Y).
- The secondary spermatocytes undergo second meiotic division to form spermatids, also carrying the haploid number of chromosomes

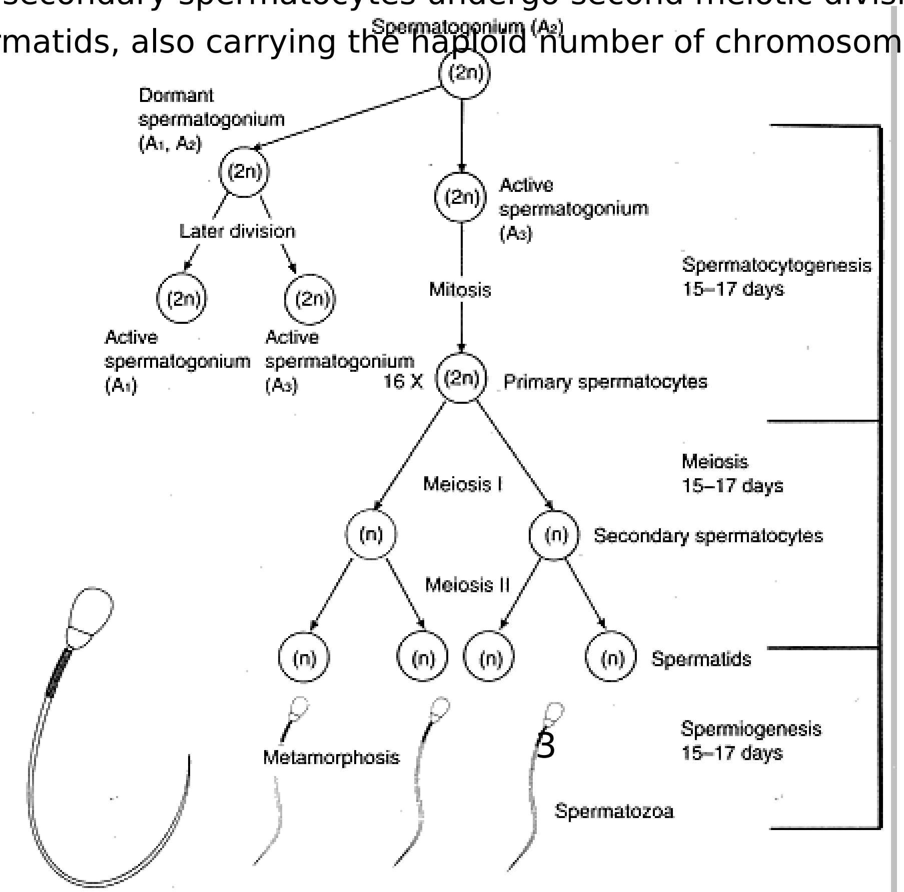


Fig. (3)

- Spermiogenesis :   : spermatids are converted without further cell division into spermatozoa. The spermatids acquire their tails and become spermatozoa, which are released in the fluid in the center of the tubule***. .***

In man, the time for a complete cycle of spermatogenesis, from the first division of spermatogonia to the release of spermatozoa is 64 days.   . . The estimated number of spermatids formed from a single spermatogonium is 512.

Until sperm maturation is complet the developing germ cells arising from single primary spermatocyte remain joined by cytoplasmic bridges allowing cytoplasm to be exchanged among the four developing sperms as X chromosom contain genes that code for cellular products essential for development of sperms,(Xcontain several thousands .Ycontain few dosen gens so if no sharing of cytoplasm the sperms carring Y are unable to survive.

Blood-Testis Barrier

It is the barrier formed by the tight junctions between adjacent Sertoli cells near the basal lamina. They prevent the passage of certain molecules from the interstitial tissue and basal compartment (part of tubule near basal lamina) to

reach the tubular lumen and vice versa. These molecules include:

1- Antigenic products resulting from spermatogenesis are prevented from entering the blood thus preventing an autoimmune response.

2- Any harmful blood-born noxious agent is prevented from reaching the tubular lumen and destroying the germ cells.

However, some substances and cells can penetrate this barrier .:

a- Testosterone

b- Maturing germ cells pass through this barrier to reach the lumen without disruption of the barrier. This occurs by progressive breakdown of the tight junctions above the germ cells, with concomitant formation of new tight junctions below them.

Tubular Fluid: It is the fluid in the lumen of the seminiferous tubules. It is formed by the Sertoli cells. It is quite different from the plasma:

- Contains very little protein and glucose.
- Rich in androgens, estrogens, K, inositol, glutamic and aspartic acids.

The presence of estrogen in the content of the fluid of rete testis (rich in estrogen receptor alpha) helps the reabsorption of water content of fluid thus concentrating the spermatozoa in a small amount of fluid, which is vital for the fertility of the spermatozoa.

Maintenance of this composition of the tubular fluid is largely dependent on the blood-testis barrier.

Functions of Sertoli Cells:

1. Nourishing and protective role:

The deep folds of the cytoplasm act as a physical support to the maturing germ cells providing them with nutrients mainly glycogen.

2. Phagocytic role:

Sertoli cells engulf any residual debris remaining from spermatogenesis.

3. Secreting role:

a- Hormones:

*1. Androgen Binding Protein (ABP)**:*** This maintains a high and stable supply of androgens in the tubular fluid.

2. Activins: which stimulate the FSH secretion from the anterior pituitary.

3. Inhibin: This inhibits the FSH secretion.

4. Mullerian Inhibitory Substance (MIS): This causes regression of the mullerian duct in the male foetus during the intra-uterine life.

5. Estrogens.

b- Enzymes: :

- Aromatase enzyme which converts androgens to estrogens.

- Proteolytic enzymes for the dissolution of tight junctions thus helping in the progress of the developing germ cells to move towards the lumen of seminiferous tubules.

- C- Tubular fluid .

4- Formation of the blood -testis barrier.

Factors affecting Spermatogenesis: (Fig. 4).

1. **Luteinizing Hormone (LH)** which acts on the interstitial cells of Leydig to produce testosterone thus maintaining spermatogenesis.

2. **Follicle stimulating hormone (FSH):**

- Acts on Sertoli cells to facilitate the last stages of spermatid maturation.

- Promotes the production of androgen-binding protein (ABP).

-Sensitizes the cells of Leydig to the LH action.

3. **Testosterone acting on Sertoli cells are essential for**:

- Spermiogenesis, i.e. maturation of spermatids to spermatozoa, although the earlier stages are androgen-independent.

- Development and maintenance of the germinal epithelium.

- Complete meiosis.

-Testosterone is ... naintain the gametogenic ...

- Producti ...
- Presenc ... ls which bi ...
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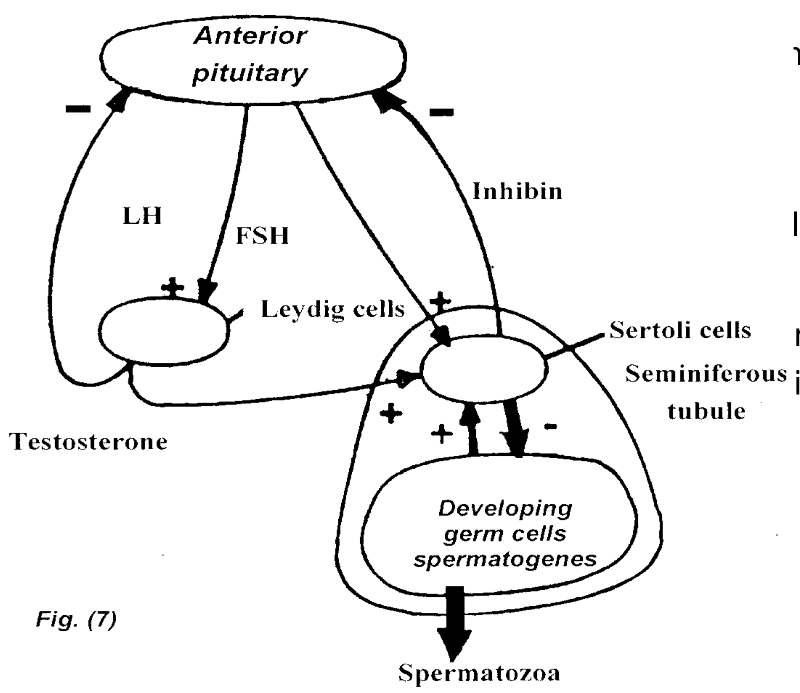


Fig. (7)

4. **Inhibins and Activins:** which regulate the secretion of FSH by anterior pituitary.

5. **Other hormones**:

-*Thyroxine*: Its decrease in cretinism or myxoedema is associated with inhibition of spermatogenesis and infertility.

-*Growth Hormone is*: important for early division of spermatogonia.

-*Leptin:* has a role in the onset of puberty and the start of spermatogenesis.

- *Estrogens* in small amounts mediate the action of FSH.

6. Temperature :

The optimum temperature for spermatogenesis is 32°C.

This lower temperature of the testicles than the body temperature is obtained through the following mechanisms:

a- Presence of the testicles in a thin-skinned scrotal sac outside the abdominal cavity.

b- Absence of subcutaneous fat in the scrotal sac.

C -Contraction of dartos muscle in cold weather to approximate the testis to the warmth of the trunk. Whereas relaxation of dartos muscle keeps the testis away from the trunk.

Hot baths at temperatures above 40° for 30 minutes, prolonged fever or tight underpants may inhibit spermatogenesis

7. Diet:

A balanced diet is essential for spermatogenesis. Vitamins A, B, C and E which are vital for spermatogenesis.

8. Factors that inhibit spermatogenesis:

- Exposure to X-rays or irradiation may cause irreversible damage of the seminiferous tubules, although the cells of Leydig maintain its secretion of testosterone.

- Bacterial, chemical toxins and O_2 lack depresses spermatogenesis.

Secondary Sex Organs

A) System of Tubules and Ducts:

Their main function is storage and conduction of spermatozoa to be propelled outside the body. They include:

a- **Epididymis:** . It is the site where storage , acquiring motility and maturation of spermatozoa are completed, until ejaculated.

b- **Vas Deferens**: muscular duct which contracts to propel the spermatozoa into the urethera. .

B) Group of Accessory Glands:

They supply the sperms with the required secretions needed for the nutrition of the sperms, . They include:

1- Seminal vesicles:

They are pairs of glands which produce a fructose rich secretion (1.5-6.5 mg/ ml); since fructose is the fuel for the sperms. It also contains ascorbic acid, prostaglandins and fibrinogen(which is changed to fibrin causing clot of semen). Their secretion constitutes 60% of seminal volume.

2. Prostate:

It secretes alkaline fluid rich in spermine, citric acid, acid phosphatase, phospholipids, cholesterol, Ca^{2+}, zinc, and proteolytic enzymes as

phosphatase, fibrinolysin whi ch dissolve seminal clot . Oxytocin is required for normal prostatic development and function. The prostate also produces prostate-specific antigen (PSA) in the semen and blood stream. PSA in the semen helps to hydrolyse semenogelin which is a sperm motility inhibitor .. Increased plasma PSA is observed in prostatitis and in benign or malignant prostatic tumors. Prostatic secretion constitutes 30% of seminal volume.

3. Cowper's glands:

Secrete mucus into the urethra which neutralizes the acidity of the urethra before ejaculation of the semen.

C) Penis:

It is the copulatory organ which delivers semen within the female genital tract. To achieve this, the penis must undergo erection and ejaculation.

Mechanism of Erection:

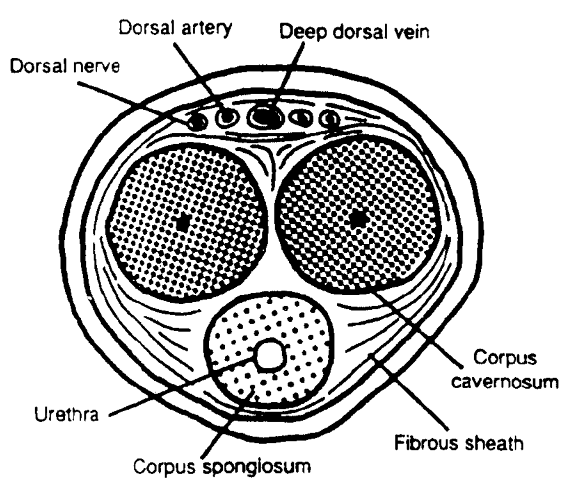
Erection is a spinal reflex..The receptors are touch receptors that are stimulated mechanically :. Centre : Sacral segments 2 ,3 ,4 .Afferent and efferent : Pelvic parasympathetic nerves . The penis contains erectile tissues . These erectile tissues consist of cavernous venous sinuses bound by fibroelastic tissue ***(Fig.5).*** During sexual intercourse, the arteries feeding the sinuses become dilated. As a consequence, there is a great increase in the blood volume flowing into the sinuses and so expand. Meanwhile, the veins that drain the sinuses are compressed and prevent blood from leaving. Thus, the penis enlarges and stiffens.

Neurotransmitters mediating erection:

- Efferent parasympathetic in the nerve eregentis produce vasodilatation of penile arteries through release of acetylcholine , VIP and NO .

- . NO increases the synthesis of cGMP which is a potent vasodilator.

Fig. (5)



N.B: ***Sildenafil (Viagra) inhibits breakdown of cGMP by phosphodiesterases especially type 5 found in corpora cavernosa, so used in treatment of impotence. However, it also inhibits PDE 6 found in the retina leading to transient loss of ability to discriminate between blue and green. Normally, erection is terminated by sympathetic vasoconstrictor impulses arriving from lumbar segments.***

Ejaculation

Ejaculation is a spinal reflex mediated by sympathetic system ; It involves :

a. Emission: it is the outpouring of semen into the urethra. Sympathetic stimulation causes contraction of smooth muscles of epididymis , vas deferens and seminal vesicles.

b. ***Ejaculation proper****:* propulsion of the semen out of the urethra at the time of orgasm. This takes place by contraction of bulbocavernosus muscle (a skeletal muscle

Human spermatozoon

A mature sperm is a motile cell, rich in DNA. It is formed of head neck body and tail:

- ***a- Head****:* made up mostly of chromosomal material. Covering the head is a cap known as acrosome. The acrosome is a lysosome-like organelle rich in enzymes involved in sperm penetration of the ovum.
- ***b- Neck***
- ***c- Body***
- ***d- A motile tail***: with the proximal portion covered by a sheath rich in mitochondria .

N.B: Its membrane contains germinal angiotensin converting enzyme with unknown function although its deffeciency may lead to infertility.

Spermiation: It is the process of completing maturation and acquiring

motility of the spermatozoa .Sperms in the tubular fluid are immotile and aquire motility in the epididymis. Spermiation is aided by:

- Contractility of myoepithelial cells lining the seminiferous tubules.
- Proteolytic enzymes released from the Sertoli cells.
- Relaxin secreted by the prostate.

The result of spermiation is the conversion of the spermatozoa into active sperms capable of movement, rich in cAMP content and forward motility hormone (FMH).

The ability to move forward (progressive motility) depends on activation of a protein called CatSper which is a calcium ion channel that permits cAMP-calcium influx ..

Capacitation:

It is the ability of the spermatozoa to fertilize an ovum. This is achieved by exposure of the sperms to the environment of the female genital tract. This involves two components:

a- Increasing the motility of the sperms

b- Facilitating their preparation for acrosomal reaction.

N.B: The role of capacitation appears to be facilitatory rather than obligatory as fertilization could occur in vitro.

Semen

It contains spermatozoa suspended in the secretions of seminal vesicles, prostate, Cowper's gland and urethral glands.

Characters of the semen:

1. Volume: 2-4 mL per ejaculate . Decreased volume and fructose content reduces fertility.
2. Colour : white and opalescent.
3. Specific gravity : 1028. Increased viscosity depresses the motility of sperms, thus decreasing fertility.

4. pH : 7.3 to 7.5.
5. Sperm count : 60-100 millions/ ml.

Oligospermia: is a low sperm count below 50 million/ml. A count below 20 million causes infertility.

Azospermia: ***absence of sperms in the semen.***

6. Sperm motility: 60% of the total sperms should be actively motile to ensure fertility. They move at speed of 3 mm/min through female genital tract reaching uterine tubes 30-60 minutes after copulation.
7. Sperm Quality: Large number of abnormal forms of sperms (double-headed, double-tailed, coiled or short tailed), is associated with infertility. ***(Fig. 9).***

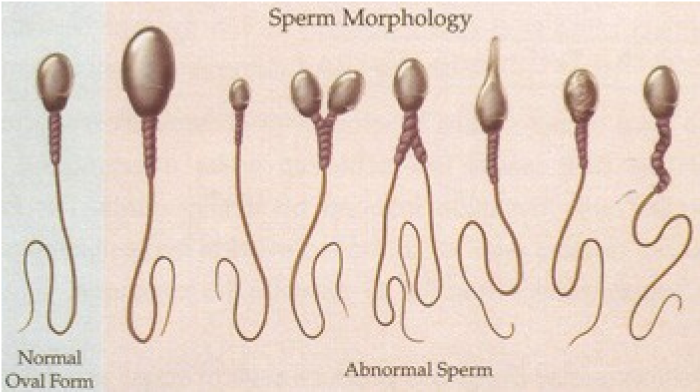


Fig. (6): Abnormal sperms

MALE HORMONES
Testosterone

Testosterone is the principal hormone (90%) of the testicular androgens. It is a C19 steroid hormone secreted from:

- Interstitial cells of Leydig in the testis.

- Adrenal cortex of both male and female, in small amounts, in response to ACTH stimulation

-In granulosa cells of the growing follicles, to be converted by aromatase to estrogen.

Precursor molecules:

1. Cholesterol in Leydig cells.

2. Androstenedione in adrenal cortex.

Secretion:

The rate of testosterone secretion is 4-9 mg/day in normal adult males. It is about 300-1000 ng/dl in adult males and 30-70 ng/dl in adult females.

Transport of testosterone in plasma:

-98% of testosterone is bound to protein in plasma: 65% to gonadal steroid-binding globulin (GBG), and 33% to albumin.

-2% is free.

Fate of testosterone

- Most of the testosterone is converted to 17-ketosteroids excreted in urine.

- A small amount is converted to estrogen, by aromatization.

- Conjugation with glucoronic acid and sulphates in the liver.

Mode of testosterone action:

-It acts as any steroid hormone by binding with intracellular receptors to form a hormone-receptor complex which binds with DNA in the nucleus, facilitating transcription of various genes.

-Testosterone can be converted to dihydrotestosterone (DHT) by **5 α -** reductase in some target cells.

Importance of DHT:

1. Binds to the same intracellular receptors of testosterone forming more stable hormone-receptor complexes than those of testosterone.
2. Descent of the testis in scotum.
3. Development and growth of external male genitalia
4. Amplifies the action of testosterone in target tissues.
5. It circulates in plasma at a level 10% that of testosterone.

Control of testosterone secretion:

A) In the intrauterine life:

In the presence of Y chromosome, the bipotential gonads at the seventh-eighth week differentiate into testicles, under the effect of a substance from the sex-determining region of Y chromosome (SRY). The embryonic testis secretes testosterone from Leydig cells. ***.***

B) The secretion of testosterone after the neonatal period ceases all through the prepubertal period due to lack of the pustile secretion of gonadal releasing hormone from hypothalamus ..

C) At puberty, the hormone is secreted in response to hypothalamic GnRH and pituitary LH. The secretion is maintained during adulthood and declines after the age of 60 years. There is a negative feedback control on testosterone secretion, since an increase in plasma testosterone inhibits release of GnRH, and LH, whereas a drop in the testosterone stimulates their release

Functions of testosterone:

A) During intrauterine life: testosterone is responsible for:

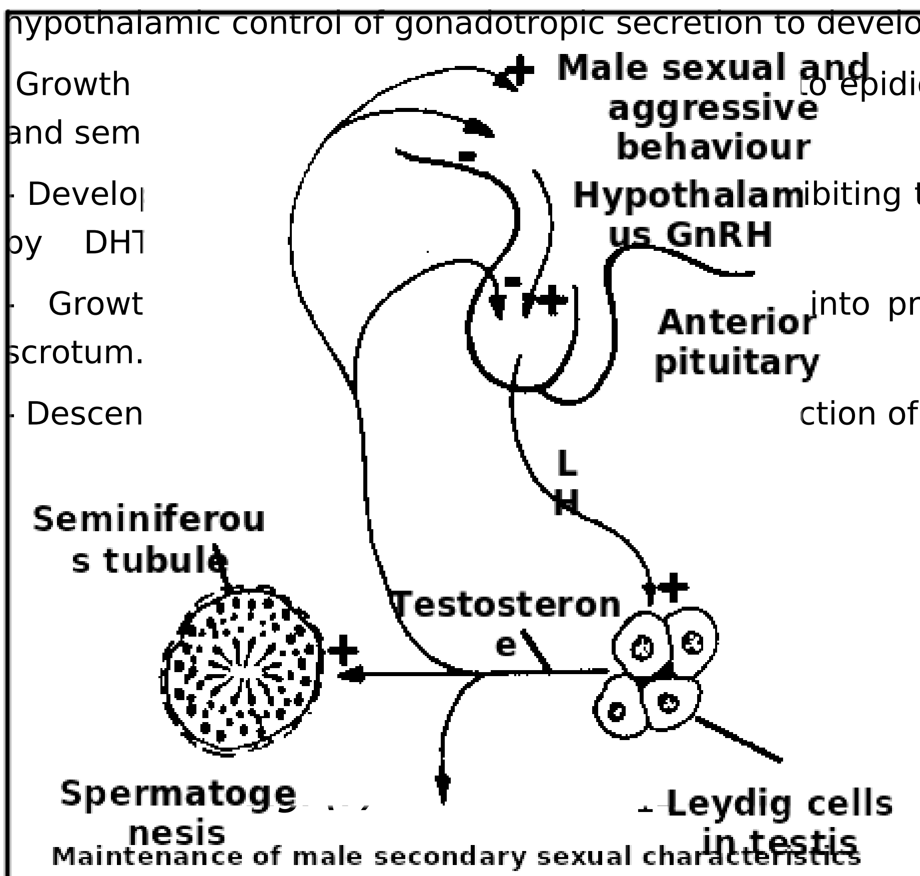
-Male pattern of sexual behavior (aggressiveness) and the male pattern of hypothalamic control of gonadotropic secretion to develop after puberty.

- Growth ... to epididymis, vas deferens and sem...

- Develo... ibiting those of the female, by DHT...

- Growt... into prostate, urethra and scrotum.

- Descen... ction of DHT.



The Role of Testosterone and its Control

B) At puberty and during adulthood:

Masculinizing Effects:

I. On the primary sex organs: testosterone is essential for spermatogenesis as mentioned before.

2. ***On the secondary sex organs:***

The seminal vesicles, prostate and Cowper's glands are largely dependent on testosterone for their growth and functions. Also the external genitalia is absolutely dependent on DHT for their development and growth.

3. Secondary sex characteristics:

- **Skin**: sebaceous gland secretion thickens and increases predisposing to acne.

- **Hair growth**: appearance of beard. Receding of hairline on scalp anterolaterally. Hair appears at the pubic region as triangle with its apex up (male escutcheon), chest, axilla, and general body hair increases.

- **Body configuration**: Shoulder broadness and muscles enlarge.

- **Voice** becomes deeper due to the increase of vocal cords in length.

Anabolic Effects:

1- Protein anabolic effect thus increasing protein synthesis in sex organs, muscles and bone, leading to an increase of muscle bulk, deposition of bone matrix and Ca^{++} salts in bones. In addition it causes increase in the growth spurt (rate of growth).

2- Moderate retention of sodium, potassium, water, sulphates and phosphates.

3- Androgens also increase the size of the viscera : kidneys , heart and liver.

4- Improve mood .

5- Cardioprotective action .

Inhibins:

- It is a protein which inhibits FSH secretion.
- Two forms of inhibins are of testicular origin in males and antral fluid of ovarian follicles in females.
- The 2 forms are: Inhibin A and Inhibin B.
- Each form is composed of 2 polypeptide units α and β. Inhibin A is composed of $\alpha\beta_A$ subunits and inhibin B is composed of $\alpha\beta_B$ subunits.

It is secreted from Sertoli cells in males and granulose cells in females.

Action:

Inhibin especially inhibin B acts directly on the pituitary to inhibit FSH. It also has an intra- ovarian action as it decreases androgen production and thus estrogen formation.

Activins:

- They are heterodimer (β_A β_B) and homodimer formed of the subunits (β_A β_A, β_B β_B).
- They stimulate FSH secretion.
- There are two types of activin receptors which are Serine Kinases. The receptors are found in:

a) Embryo: it indicates that activin is involved in mesodermal formation.

b) Gonads.

c) Brain.

d) Bone marrow: activins are involved in white blood cells development.

In plasma; α_2-macroglobulin is found to bind to activins and inhibins. In tissues; activins bind to follistatins (glycoproteins) to inactivate the biologically active activins. However, follistatins' relation to inhibins is still unsettled.

TESTICULAR FUNCTION TESTS

1) Semen analysis .

2) Estimation of urinary gonadotropins: these are the pituitary gonadotropins which are secreted in urine. They are useful for the differentiation between primary and secondary hypogonadism.

- In primary hypogonadism: gonadotropins are high (no feed-back).
- In secondary hypogonadism gonadotropins are low (the pituitary is non-functioning).

3) Estimation of 17- Ketosteroids in urine: 2/3 of the 17- Ketosteroids are from the cortex (corticosteroids and androgens). While 1/3 of the 17-Ketosteroids is the testicular androgens.

- They decrease in impairment of Leydig cell function.
- A sterile is with normal 17-ketosteroids level indicates absence of gametogenic activity.

4) Estimation of blood testosterone level, FSH and LH.

- A decrease in testosterone and gonadotropins (FSH & LH) blood levels denote hypogonadism secondary to pituitary or hypothalamic causes.
- A decrease in testosterone with a high gonadotropin level denotes primary hypogonadism

5) Testicular biopsy: Is done in cases of azospermia A Sample of testicular tissue is examined histologically.

- If the seminiferous tubules contain sperms, this denotes duct

obstruction.

- If the seminiferous tubules contain no sperms this denotes absence of gametogenic activity.

Abnormalities of Testicular Function: -

[1] Cryptorchidism:

- It is failure of testicular descent in the scrotum during fetal life.
- It occurs in 10% of new born infants. It falls to 2% by the age of 1 year and 0.3% at puberty.
- Descent of testis in scrotum depends mainly on testosterone and MIS.

Treatment: -

1- Gonadotropic hormone administration speeds the descent in some cases.

2- Surgical treatment:

Complications of cryptorchidism:-

a- Higher incidence of malignant tumors in undescended testis than scrotal testis.

b- Irreversible damage to spermatogenic epithelium of testis, due to higher temperature in abdomen.However , Leydig cells are not affected .

[2] Male Hypogonadism: -

Depends upon whether testicular deficiency develops before or after puberty.

Causes of hypogonadism: -

1- Local disease in testis.
2- Surgical castration
3- Disorder in hypothalamic - pituitary axis suppressing the gonadotropins.

[A] Before puberty: -

The clinical picture due to Leyding cell deficiency in childhood is called eunuchoidism.

The eunchoid individuals have the following characters:-

a) ***Tall stature:-*** because their epiphysis remain open post the normal age of puberty leading to some growth till age of 20

b) ***Narrow shoulders and small muscles:*** with a body configuration similar to an adult female.

c) Small genitalia and high-pitched voice.

d) ***Sparse axillary and pubic hair*** with the distribution of the hair of the latter in the form of female triangle.

[B] After puberty: -

- If it is due to testicular disease; the gonadotropin levels circulating in the blood are elevated (hypergonadotropic hypogonadism).
- If it is secondary to disorders of the pituitary or hypothalamus, then the circulating gonadotropin levels are depressed (hypogonadotrpic hypogonadism).

The secondary sex characters regress slowly since they need little testosterone for their maintenance. The growth of the larynx during adolescence is permanent and the voice remains deep.

- If it is second to castration, it leads to loss of libido, hot flushes, depression and irritability.

[3] Congenital 5-α-reductase deficiency: -

5- α-reductase is an enzyme needed for the conversion of testosterone to DHT

Congenital 5-α reductase deficiency is due to gene mutation , leading to male pseudohermaphroditism (male internal genitalia and female external genitalia).